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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.		
10/672,225	09/26/2003	Ivan Alferiev	RCHP-125US1	2873		
23122	7590	12/07/2009	EXAMINER			
RATNERPRESTIA P.O. BOX 980 VALLEY FORGE, PA 19482				LUM, LEON YUN BON		
ART UNIT		PAPER NUMBER				
1641						
MAIL DATE		DELIVERY MODE				
12/07/2009		PAPER				

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)
	10/672,225	ALFERIEV ET AL.
	Examiner	Art Unit
	Leon Y. Lum	1641

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 09 July 2009.
 2a) This action is **FINAL**. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-31 is/are pending in the application.
 4a) Of the above claim(s) 4,8-13,15,17,21 and 23-30 is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 1-3,5-7,14,16,18-20,22 and 31 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on 12 March 2007 is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ . |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____. | 6) <input type="checkbox"/> Other: _____ . |

DETAILED ACTION

Status of Claims

Claims 1-31 are pending, with claims 4, 8-13, 15, 17, 21 and 23-30 withdrawn.

Claims 1-3, 5-7, 14, 16, 18-20, 22 and 31 are examined on the merits.

Priority

The instant application is a CIP of U.S. Patent App. No. 10/170,411, now U.S. Patent No. 7,589,070, which claims the benefit of U.S. Provisional App. No. 60/298,116. The application also claims the benefit of U.S. Provisional App. No. 60/413,460. Neither the '070 patent nor the '116 application describe the claimed method embodied in claim 1. Accordingly, for prior art purposes, priority is given only to the '460 application, filed September 26, 2002.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 5-7, 14, 16, 18-19 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,399,501 to Pope *et al.* ("Pope") in view of U.S. Patent No. 6,977,722 to Wohlstadter *et al.* ("Wohlstadter") and U.S. Patent No. 4,318,981 to Burd *et al.* ("Burd").

i. Independent claim 1 is obvious

Pope describes a process of modifying a solid phase with a coupling agent. See column 3, lines 38-53; column 9, lines 32-48; Figure 6. The solid phase can have a dithiol group "X". *Id.* The dithiol group attaches to coupling agent "R'," which is a heterobifunctional group. See column 3, lines 48-50. The heterobifunctional group can include thiol-cleavable agents such as N, N'-didansyl-L-cysteine. See column 7, lines

46-49. Figure 6 depicts the cleavage of R'. With this description, Pope teaches the "providing," "contacting," and "cleaving" steps as claimed.

Pope, however, does not teach the "exposing," "measuring" and "calculating" steps.

Wohlstadter describes a method of detecting cleaved labels in order to detect binding between two molecules. See column 104, lines 51-67. Note: Wohlstadter has priority to June 29, 2001, which is an earlier date than the benefit accorded to the instant application. See *supra* description on priority.

Burd describes a process for determining the binding capacity of a ligand. See abstract.

With the foregoing description in mind, one of ordinary skill in the art would have found it obvious to modify Pope's method to detect the thiol-cleavable agents for the purpose of determining binding capacity. The skilled artisan would have made the modification because Wohlstadter indicates that cleaved labels can be used to determine detect binding between two molecules. The skilled artisan would have recognized the benefit of applying Wohlstadter's technique to determine whether the coupling agent binds to the solid phase. Moreover, Burd indicates that cleaved labels can be used to determine binding capacity between two molecules. Accordingly, the skilled artisan would have recognized the benefit of applying Burd's technique to determine, from the cleaved label, how strongly the coupling agent binds to the solid phase. Furthermore, although Wohlstadter and Burd are directed towards biomolecule binding and Pope is directed to surface modification, the former references can be

appropriately combined with Pope because their teachings are relevant to whether Pope's coupling agent effectively modifies and binds to the solid phase. For the same reason, the skilled artisan would have had a reasonable expectation of success in combining the references.

ii. Dependent claims 2-3, 5-7, 14, 16, 18-19 and 31 are obvious

Regarding claims 2 and 3, Pope describes a disulfide bond that is cleaved. See Figure 6.

Regarding claims 5-7, Pope teaches N, N'-didansyl-L-cysteine, as described above.

Regarding claim 14, the solid phase can be a polymer. See column 6, line 44.

Regarding claims 16 and 18-19, Pope teaches the dithiol group described above.

Regarding claim 31, Wohlstadter teaches a washing step after introducing a label. See column 92, line 16.

Claims 20 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pope in view of Wohlstadter and Burd as applied to claims 1 and 2 above, and further in view of Burns *et al.* J. Org. Chem. (1991) 56:2548-2650 (“Burns”), already of record.

Pope, Wohlstadter and Burd (together “Pope”), described above, do not teach tris(2-carboxyethyl)phosphine.

Burns describes tris(2- carbodyethyl)phosphine hydrochloride (TCEP) as a reducing agent that rapidly and complete reduces disulfide bonds. See abstract.

With the foregoing description in mind, one of ordinary skill in the art would have found it obvious to modify Pope's method by using TCEP as the reducing agent. The skilled artisan would have been motivated to use TCEP since Burns indicates that the compound can act quickly and to completion. Because Pope's cleavable bond is a disulfide bond, the skilled artisan would have recognized that applicability of TCEP to Pope's method. For the same reason, the skilled artisan would have had a reasonable expectation of success.

Response to Arguments

Applicants' arguments, see pages 9-11, filed July 9, 2009, with respect to the rejections of the pending claims have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground of rejection is made in view of Pope in view of Wohlstadter and Burd. See *supra* rejections. Because a new ground of rejection is not made in response to a claim amendment, this action is being made non-final.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y. Lum whose telephone number is (571) 272-

2872. The examiner can normally be reached on Monday to Friday (8:30 am to 5:00 pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark L. Shibuya can be reached on (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon Y. Lum/
Examiner, Art Unit 1641

/Unsu Jung/
Primary Examiner, Art Unit 1641